Amendments to the Specification

Please replace the paragraph beginning at page 2 line 17, with the following amended paragraph:

As mentioned above, it is known that immunosuppressants FK506 and cyclosporine A have a suppressive effect on neuronal cell death, in particular ischemic and excitatory neuronal cell death. However, it is known that the side effect of such agents is large (for example, toxicity, ~~diabetic~~ diabetes and the like), because the agents suppress all signal transduction involved in calcineurin. Therefore, a suppressant for neuronal cell death which can inhibit a long term activation of calcineurin and show less side effect compared with the conventional one is strongly desired.

Please replace the paragraph beginning at page 3 line 2, with the following amended paragraph:

The objects of the present invention are to solve the above-mentioned problems and to provide a suppressant for neuronal cell death having less side effect and which is effective for treating various diseases.

Please replace the paragraph beginning at page 3 line 13, with the following amended paragraph:

c) It was clarified that calcineurin had an activity ~~independently~~independent of calcium and calmodulin, when it was cleaved at said sites.

Please replace the paragraph beginning at page 3 line 19, with the following amended paragraph:

e) When the peptide including amino acid residues 392-393 or amino acid residues 421-425 of CaNA was introduced in the neuronal cell, neuronal cell death by ~~the~~ glutamic acid administration was suppressed.

Please replace the paragraph beginning at page 5 line 6, with the following amended paragraph:

The above-mentioned analogue of the peptide of SEQ No. 1 includes a peptide comprising amino acid sequence of the peptide of SEQ No. 1 which is deleted, substituted a part thereof and/or another amino acid sequence is inserted or added at the terminal of the peptide, and which inhibits cleavage of CaNA by calpain. For example, a peptide ~~changed~~ in which the amino acid residue 9 is changed from Arg to Lys and/or a peptide ~~changed~~ in which the amino acid residue 10 Lys is changed to Arg in the peptide of SEQ No. 1 ~~are~~ is included in the ~~analogue~~analogues of the peptide of SEQ No. 1 of the present invention.

Please replace the paragraph beginning at page 5 line 15, with the following amended paragraph:

The above-mentioned analogue of the peptide of SEQ No. 2 includes a peptide comprising amino acid sequence of the peptide of SEQ No. 2 which is deleted, substituted a part thereof and/or another amino acid sequence is inserted or

added at the terminal of the peptide, which inhibits cleavage of CaNA by calpain. For example, a peptide ~~changed~~ in which the amino acid residue 11 Lys is changed to Arg in the peptide of SEQ No. 2 ~~are~~ is included in the ~~analogue~~ analogues of the peptide of SEQ No. 2 of the present invention.

Please replace the paragraph beginning at page 6 line 13, with the following amended paragraph:

The inhibitor for cleavage of CaNA by calpain of the present invention can contain an additional compound as long as it contains the peptide of SEQ No. 1, the peptide of SEQ No. 2 and/or the analogue thereof. The additional compound includes, for example, an intracellular transporting signal peptide consisting of 7 to 30 amino acid residues which contains 50 % or more arginine or lysine thereof, such as a polyarginine peptide (for example, polyarginine peptide consisting of five arginine residues), protein transporting domain (PTD; SEQ No. 4) consisting of 11 amino acid residues which is contained in TAT protein of HIV virus; or ~~liner~~ linear polyethylenimine (PEI) being a cationic water-soluble polymer. Such compound can be associated with (or fused to) the peptide of SEQ No. 1, the peptide of SEQ No. 2 and/or the analogue thereof by using a method such as (i) to be synthesized starting with the peptide of SEQ No. 1, the peptide of SEQ No. 2 and/or the analogue thereof using general peptide synthesis, or (ii) one peptide is bound to a divalent

crosslinking agent, a terminal of another peptide is bound to a cysteine residue, and then ~~the~~ both ~~peptide~~ peptides ~~is~~ are reacted. The thus obtained inhibitor for cleavage of CaNA can be purified with the above-mentioned purification method.

Please replace the paragraph beginning at page 7 line 5, with the following amended paragraph:

The suppressant for neuronal cell death of the present invention means an agent which comprises the above-mentioned inhibitor for cleavage of CaNA by calpain as an active ingredient, and inhibits long term induction of neuronal cell death in neuronal cells. The suppressant for neuronal cell death can be also used as an agent for preventing or treating a disease related to neuronal cell death. The suppressant for neuronal cell death of the present invention preferably contains the inhibitor for cleavage of CaNA comprising the peptide of SEQ No. 2 and the intracellular transporting signal peptide, and more preferably contains the inhibitor for cleavage of CaNA comprising the peptide of SEQ No. 1, the peptide of SEQ No. 2 and an intracellular transporting signal peptide. The above-mentioned agent for preventing or treating a disease related to neuronal cell death means a pharmaceutical preparation comprising an effective amount of the suppressant for neuronal cell death for preventing or treating the disease related to neuronal cell death. The disease related to neuronal cell death

includes, for example, Alzheimer's disease, dementia ~~disease~~, brain ischemic disease, intracerebral hemorrhage such as subarachnoid hemorrhage, spinal injury (trauma), Parkinson disease, ~~epilepsys~~epilepsy, and the like.

Please replace the paragraph beginning at page 7 line 25, with the following amended paragraph:

As an administration route of the suppressant for neuronal cell death of the present invention, there include, for example, oral administration, intravenous administration, intracerebral ~~directly~~ direct administration and the like. The oral administration is ~~more~~ preferable in the light of a burden on a patient and the side effect.

Please replace the paragraph beginning at page 8 line 27, with the following amended paragraph:

An additive for a culture medium of cells and brain slice comprising of the present invention means the additive for the culture medium containing at least the inhibitor for cleavage of CaNA. The additive for the culture medium of cell and brain slice comprising ~~of~~ the present invention preferably contains the inhibitor for cleavage of CaNA comprising the peptide of SEQ No. 2 and the intracellular transporting signal peptide, and more preferably contains the inhibitor for cleavage of CaNA comprising the peptide of SEQ No. 1, the peptide of SEQ No. 2 and an intracellular transporting signal peptide.

Please replace the paragraph beginning at page 9 line 20, with the following amended paragraph:

In order to introduce FDGATAAARKEVIRNK (SEQ No. 1) and REESESVLTLKGLTPTG (SEQ No. 2) as the inhibitor for cleavage of CaNA of the present invention into the cultured cells, the following oligopeptides in which the intracellular introducing signal peptide (ten arginines) was added to their N terminal were prepared (available ~~form~~ from PEPTIDE INSTITUTE INC.).

Please replace the paragraph beginning at page 10 line 2, with the following amended paragraph:

After the brain hippocampus from 18 days embryo of Wister rat had been removed, it was treated with PBS containing 0.05 % trypsin for 15 minutes at 37°C. After the neuronal cells were suspended with a glass pipet, 1×10^6 cells were cultured in a 3.5 cm ~~in the~~ diameter culture dish which was previously coated with poly-D-lysine. As the medium, 3 ml Neuro Basal medium (available ~~form~~ from Invitrogen, Inc.) complemented with B27 supplement (0.03 ml; available from Invitrogen, Inc.), penicillin (100 units/ml in the final concentration; available ~~form~~ from Invitrogen, Inc.) and streptomycin (100 µg/ml in the final concentration; available ~~form~~ from Invitrogen, Inc.) was used and the cultivation was carried out in carbon dioxide incubator (5 % CO_2, 37°C).

Please replace the paragraph beginning at page 10 line 16, with the following amended paragraph:

The peptides of above-mentioned SEQ Nos. 5 and 6 were added in the culture solution with the final concentration of 1 μM 10 days after beginning of culture, and it was incubated in carbon dioxide incubator (5 % CO_2, 37°C). Three hours after the addition, glutamic acid was added in the final concentration of 500 μM, and it was incubated for 15 minutes. The culture solution was then exchanged, and it was further cultured. The cells were collected at 3 hours and 24 hours after glutamic acid was added, were disrupted by ultrasonic wave in 1 % SDS solution, and the SDS-PAGE buffer was added thereto. After this sample was subjected to the SDS-PAGE gel electrophoresis, Western blotting was carried out using the antibody recognizing CaNA (rabbit serum, available ~~form~~ from Santa Cruz Biotechnology, Inc). In this Example, a cell sample in which neither glutamic acid nor the cleavage inhibiting peptide was added was used as a control. Moreover, the cell sample in which only glutamic acid was added and the cell sample in which only the cleavage inhibiting peptide was added were concurrently prepared.